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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,883	02/12/2004	Alexander V. Chervonsky	JMY-P01-001	6714

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EXAMINER	
STANDLEY, STEVEN H	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 09/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/777,883	CHERVONSKY ET AL.	
	Examiner	Art Unit	
	Steven H. Standley	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/6/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *7,8 and 10-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I (claims 1-10), CCR7, and a mutated form or mimic of CCL21, in the reply filed on 6/06/05 is acknowledged. The traversal is on the ground(s) that examination of Groups I and II, in particular, will not pose a substantial burden on the examiner. This is not found persuasive because group I and group II are directed to modulating the homing of T-cells to the pancreas by distinct and unrelated means. The reagents and targets are entirely different, and therefore the searches would not be coextensive, placing a significant and serious burden upon the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7, 8, and 10-48 are withdrawn from consideration, as they are directed to non-elected inventions or species.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Claim Objections

3. Claims 1-6 and 9 are objected to because of the following informalities: They contain reference to 'CCL21,' and 'CCR7,' without first disclosing the meaning of the acronyms in the claims. In order to make the description of the invention more clear, the first claim that mentions these acronyms should fully express the phrase, and be followed by parentheses, which identify the acronym to be used in the following claim(s). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3, 5-6, and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting the homing of insulin-sensitive CD8+ T-cells by administration of pertussis toxin or an anti-CCL21 (SLC; purchased from R&D systems) antibody, or an N-terminally truncated SLC which antagonizes SLC binding to CCR7, or the N-terminally truncated CCL21 antagonist of the prior art (see Sasaki et al, 2003), does not reasonably provide enablement for modulating the homing of T-cells to pancreas by administration of an agonist or antagonist of the chemokine CCL21 (SLC), including mutated or mimic forms of CCL21. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is a method of modulating the homing of T-cells to the pancreas by administering an agonist or antagonist that modulates CCL21 activity in an amount sufficient to modulate the homing of T-cells to the pancreas. This is a complex biological process involving many receptors, secreted factors, and cell types.

The prior art discloses that N-terminally truncating the CCL21 chemokine results in the creation of a CCL21 antagonist (Sasaki et al., January, 2003), that pertussis toxin prevents signal transduction through chemokine receptors (Suzuki et al, 1999), and administration of an antibody to CCL21 (SLC) inhibits CCL21 activity (Engenman et al., 2000). The prior art does not disclose CCL21 "agonists" or "modulators," or CCR7 "agonists" or "modulators," other than CCL21 itself as the native agonist of CCR7. Furthermore, the prior art does not teach any administration or use of such "agonists" for "modulating" the homing of T-cells; the prior art does not teach "modulating" the homing of T-cells—it teaches *inhibiting* the homing of T-cells, and the properties that any new compound might have with respect to CCL21 activity are highly unpredictable.

The working examples disclose using pertussis toxin (which is an antagonist to the G-protein subtypes 'Gi' and 'Go') to inhibit signal transduction through CCR7, or an antibody to CCL21 to *inhibit* CCL21 action on CCR7, and thereby inhibit homing of insulin-sensitive T-cells to the pancreas. There are no working examples of any agonist or antagonist otherwise. Thus, notwithstanding an antibody to CCL21, a few N-terminal truncations of CCL21 disclosed in the prior art, neither the specification nor the prior art teach additional "antagonists" and do not teach any "agonists" or what such "agonists" would be used for. Additionally, there are no other teachings or guidance in the specification as to what constitutes an "agonist" or "antagonist" for the modulating T-cell homing, nor does the specification give guidance for activating or facilitating T-cell homing through the use of anything. Therefore the specification does not teach one of skill in the art "modulating" of T-cell homing in its appropriate scope, which includes both activating or facilitating or inhibiting of T-cell homing.

The breadth of the claims are such that one skilled in the art cannot make or use "agonists" or "antagonists" for inhibiting, much less "modulating" the homing of T-cells, because the agonist and antagonists are only defined functionally, with not structural limitations.

Thus, given the complex nature of the invention, the state of the art, the lack of guidance in both the examples and specification, the unpredictability of what activity a new compound may have, and the breadth of the claims, one skilled in the art could not make or use the invention as currently claimed without undue experimentation.

5. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claim 4 is a method of modulating homing of T-cells to the pancreas by contacting the cells with an agonist or antagonist of the chemokine CCL21, wherein the agonist or antagonist modulates CCL21 expression. This is a complex biological process involving many receptors, secreted factors, and cell types.

The prior art provides for no compound or drug that modulates (i.e., agonizes or antagonizes) *expression* of CCL21, nor does it suggest its usefulness in modulating of the homing of T-cells, and the effect any new compound would have on CCL21 expression is highly unpredictable.

The specification provides no agonist or antagonist that modulates the expression of CCL21, nor does it provide any evidence by way of examples or guidance

for the making or usefulness of modulating CCL21 expression in the modulating of T-cell homing to the pancreas.

The breadth of the claims are such that one skilled in the art would not know how to make or use an agonist or antagonist of CCL21 for modulating T-cell homing to the pancreas. No structural limitations are recited, and the functional limitation includes both inhibition and enhancement.

Thus, given the nature of the invention, the state of the prior art, the lack of any guidance by way of working examples or disclosure in the specification and the breadth of the claims, one skilled in the art would not know how to make or use the invention of claim 4.

6. Claims 1-6, and 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No written description is provided in the instant specification as to what structurally constitutes an agonist, antagonist, a modulator, a mutant or a mimic of CCL21. The specification has not described, nor can it be reasonably visualized by one skilled in the art, the structural and functional elements attributable agonists, antagonists, modulators, mutants, or mimics of CCL21, which represents a potentially

enormous number of undisclosed and undefined organic or inorganic compounds, polypeptides, or nucleic acids.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers* v. *Revel*, 25 USPQ2d 1601 at 1606 (CMC 1993) and *Amgen Inc.* v. *Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore only the disclosed pertussis toxin, R&D antibody to CCL21, and the N-terminal truncations of CCL21 of Sasaki et al meet the written description requirement, and not the full scope of what is claimed.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-3, 5-6, and 9 rejected under 35 U.S.C. 102(a) as being anticipated by Sasaki et al., (January 1, 2003).

Sasaki et al. report the administration of truncated forms of CCL21 that are antagonists to animals. Sasaki et al administered 50 micrograms/ml of mSLC-4, a CCL21 antagonist, to mice (see page 591, left column, Sasaki et al.). This was sufficient to block CCR7 receptor expressing T-cells form homing to lymphoid tissue (see abstract). Therefore, absent evidence to the contrary, the administration was also sufficient to block T-cell homing to the pancreas, meeting the limitations of claims 1. mSLC-4 also binds and antagonizes CCL21 function, activity, and interaction with CCR7, meeting the limitations of claims 2-3, and 5-6. mSLC-4 is a mutant of CCL21, meeting the limitation of claim 9 (see figure 1, Sasaki et al.).

9. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Hermida et al., 1991.

Hermida et al. disclose administering pertussis toxin, which interferes with the function of the CCR7 G-protein, to rats (see Hermida et al., page 1301, both in vivo and in vitro experiments). Absent evidence to the contrary, this is also sufficient to block CCL21-mediated signaling through CCR7, which would also reasonably inhibit homing of T-cells to the pancreas.

10. Claims 1-3, and 5-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Engeman et al., 2000.

Engeman et al. administer the same antibody as disclosed in the specification (R&D systems) to mice at a dose of 100 micrograms, twice the dose reported in the

specification as given to NOD mice (page 41, 30-50 micrograms). This is clearly sufficient to also inhibit CCL21 activity and function by inhibiting interaction and signaling through CCR7, which meets the limitations of claims 1-3, and 5-6.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Suzuki et al. indicated pertussis toxin blocks chemokine receptor CCR7 function.

Conclusion

No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Standley whose telephone number is **(571) 272-3432**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on **(571) 272-0867**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Steve Standley, Ph.D.
8/24/05

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER